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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,142	07/19/2000	W. Ray Knowles	Knowles/HairLoss	1598
22925	7590	07/01/2004		
PHARMACEUTICAL PATENT ATTORNEYS, POHL & ASSOC. 55 MADISON AVENUE, 4TH FLOOR ATTN: MARK POHL (P 4014) MORRISTOWN, NJ 07960-6397			EXAMINER KIM, VICKIE Y	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.



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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 09/619,142
Filing Date: 19 July 2000
Appellant(s): W. Roy KNOWLES, M.D.

~~Paper No. 34~~
No. 37
MAILED
JUL 1 - 2004
GROUP

MARK POHL
For Appellant

SUPPLEMENTAL EXAMINER'S ANSWER

This is in response to the APPEAL BRIEF filed July 18, 2003. Thus, the instant office action(Examiner's Answer) supercedes any previous office action.

(1) ***Real Party in Interest***

A statement identifying the real party in interest, Knolltech Pharmaceutical, Inc., is contained in the brief.

(2) ***Related Appeals and Interferences***

The petition for writ of mandamus in this case has been filed with the court if Appeals for the Federal Circuit. The court, however, denied the mandamus petition and dismissed any appeal to the CAFC filed by Knowles (order of August 1, 2003).

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct in noting that there are not pending amendments.

(5) Summary of Invention

The invention is drawn to a composition and a method for maintaining healthy hair and preventing abnormal hair loss, by using said composition, wherein the composition comprising minoxidil or a 5 α -reductase inhibitor as an active agent, and a skin penetration enhancer. Optionally, the invention comprises a combination of minoxidil and 5 α -reductase inhibitor with a skin penetration enhancer. For instance, claim 1 recites, " 1. A composition of matter intended for topical use in preventing or treating alopecia, or maintaining healthy hair, said composition of matter comprising: (a) an active compound selected from the group consisting of : a pharmaceutically or cosmetically effective topical amount of a 5 α -reductase inhibitor and minoxidil, and (b) a non-retinoid penetration enhancer, said penetration enhancer present in a concentration sufficient to aid said active compound in penetrating the skin surface to a depth of approximately the depth of hair bulbs."

However, appellant states that the claims are drawn to a combination of minoxidil and a 5 α -reductase inhibitor with a skin penetration enhancer (page 4, lines 25-26). The claims 1-3 and 12-14 utilize the composition comprising only one active agent selected from either minoxidil or a 5 α -reductase inhibitor whereas only claims 4-11 and 15-22 utilize a combination of both minoxidil and testosterone blocker or inhibitor as active agents in the treatment of preventing or treating alopecia. Thus, the statement included in the summary of invention is partially correct.

(6) Issues

The appellant's statement of the issues in the brief (page 5) is not accurate. The appellant's statement presents that the issues are whether the cited references anticipate the claims when said references do not specifically mention about the claimed recitation (i.e. penetration to a depth of approximately the depth of hair bulbs).

However, the issues should be directed to whether all the critical elements required by the instant claims including the specific concentration as claimed are taught by the cited references? Because the limitation recited in preambles (i.e. penetration to a depth of approximately the depth of hair bulbs) is considered to be an inherent feature which would be naturally achieved when the concentration of the penetration enhancer as claimed is met.

Thus, the issues remained in the case should be related to whether the cited reference teaches all the critical elements required by the instant elements.

(7) Grouping of Claims

The appellant's statement regarding grouping of claims in the brief is not clear (page 6, last paragraph). Appellant indicates that the claims are each separately patentable as explained in detail in the following argument. However, different group of claims are argued together in separate arguments, it is not clear how appellant is grouping the claims.

Recommended grouping of the claims are as following:

(i) claims 1-3: a composition comprising only one active agent selected from either minoxidil or a testosterone blocker (inhibitor) with an therapeutically effective concentration of penetration enhancer.

(ii) claims 4-7: a combination composition having both minoxidil and testosterone blocker (or inhibitor) and an therapeutically effective concentration of penetration enhancer.

(iii) claims 8-11: a article comprising a composition of group (ii) and a label for topical use.

(iv) claims 12-14: a method for preventing or treating alopecia, or maintaining healthy hair using the composition according to the claims of group (i).

(v) claims 15-22: a method for preventing or treating alopecia, or maintaining healthy hair using the composition according to the claims of group (ii).

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

It is noted that the clerical error was found in claim 5 wherein "penetration enhancer to" right before :5 α reductase inhibitor" was undeleted inadvertently. As evidenced by amendment(paper 20), the phrase "penetration enhancer to" should have been deleted from the claim 5 as marked.

(9) Prior Art of Record

The prior art of record contained in the brief is correct.

5,183,817	Bazzano	Feb. 02, 1993
5,015,470	Gibson	May 14, 1991
5,192,534	Grollier	Mar. 09,1993
5,373,012	Schostarez	Dec. 13,1994
4,440,777	Zupan	Apr. 03,1984
Transdermal delivery and accumulation...	Mikulak et al	1998(abstract only)

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

- a. All pending claims are rejected under 35 U.S.C. 112, first paragraph, because the newly introduced limitation(i.e. a non-retinoid penetration enhancer) recited in the claim 1 is considered to be a "new matter" wherein said limitation is not supported by the original disclosure or there is no pertinent teaching of retinoid penetration enhancer(s) or exclusion of retinoid penetration enhancer(s) in the original disclosure.

b. Claims 1-4 and 12-15 stand rejected as anticipated by BAZZANO(US .

This rejection is summarized as follows:

The claims 1-4 are drawn a composition comprising (a) a pharmaceutically or cosmetically effective topical amount of a 5 α -reductase inhibitor and minoxidil, and (b) a non-retinoid penetration enhancer, said penetration enhancer present in a concentration sufficient to aid said active compound in penetrating the skin surface to a depth of approximately the depth of hair bulbs.

The claims 12-15 teaches a method for maintaining healthy hair and preventing abnormal hair loss, by using said composition.

Bazzano teaches a composition comprising minoxidil, retinoid(e.g. retinoic acid) wherein the effective amount of about 0.1-30% minoxidil and 0.001-2% of retinoid are used, see abstract and page column 20, lines 54-64. Bazzano teaches that retinoid cause excellent percutaneous absorption of themselves and other compounds used in combination therewith and are very active on the hair follicles, see column 19, lines 35-42. Bazzano further teaches progesterone or other antiandrogens in combination with the said composition of minoxidil and retinoid wherein said antiandrogens including progesterone acts on the nucleous of the hair follicle cells, see claims 28-29 and column 20, lines 15-20.

Bazzano also teaches a method of treating alopecia due to dysfunction of hair follicle by topical application of said composition to hair, hair follicles and to the skin adjacent thereto, see claim 13 and column 3, lines 60-65.

Progesterone is conventionally known to be an antiandrogen that inhibit 5-alpha reductase activity, as evidenced by (Orentreich et al(US5053403, column 2, lines 10-15 and also discussed in previous office action, see paper 5) . Thus, the claimed subject matter(i.e. a combination of minoxidil or 5- α reductase inhibitor, optionally, or the mixture thereof ; and a penetration enhancer) is inherently met by the combination of minoxidil, retinoid and progesterone taught by Bazzano.

Thus, all the critical elements are taught by the cited reference and the claimed subject matter is not patentably distinct over the prior art of the record.

c. Claims 1, 3,12 and 14 are rejected as anticipated by Gibson(US5015470).

Gibson teaches a topical composition for maintaining and increasing hair growth comprising minoxidil and a penetration enhancers(see abstract, table 1 and col. 4, lines 40-42). It further teaches that said penetration enhancer potentiates the benefit of the chemical(i.e. monoxidil) by improving it's delivery through the stratum corneum to the site of action in the immediate environment of the hair follicles, see column 14, lines 1-15(emphasis added). Thus, all the critical elements required by the instant claims are well taught and met by the cited reference.

In response to the appellant's argument, appellant is reminded that the claims are direct to a composition set forth above and it's use in the treatment of alopecia the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the

intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

d. Claims 1-2, 12 and 13 are rejected as anticipated by Zupan(US 4,440,777).

Zupan teaches a progesterone in combination with eucalyptol(or other penetration enhancers) for treating alopecia wherein said eucalyptol is used as a penetration enhancer to deliver the active agent to the targeted site effectively without toxic side effect, see abstract and column 3, lines 17-35 and column 6, lines 37-43. As evidenced by Bazzano's reference, it is known in the art that the active working site of progesterone is hair follicle, see column 20, lines 15-20. Regardless of knowing that active working site of progesterone is hair follicle, the claimed subject matter is inherently met by the teaching of the cited reference since all the critical elements (5-alpha reductase inhibitor(i.e. progesterone) and a therapeutically effective concentration of penetration enhancer for improving penetration (delivery) to the active working site) are well taught. Thus, one would have envisaged the claimed subject matter from the teaching of Zupan's patent.

Thus, the claimed subject matter is not patentably distinguished from the cited reference.

e. Claims 2, 4-5, 7-10, 13, 15-16, 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gibson (US 5,015,470) in view of Bazzano (US 5183817) or Schostarez (US 5,373,012).

Gibson's teaching is mentioned in 102 rejection (Supra). Gibson also suggests that the additional benefit can be obtained by combining other hair growth stimulants, see column 12.

Applicant's claims differ because Gibson fails to teach 5 alpha reductase inhibitor as the hair growth stimulant required to make a combination composition.

However, it would have been obvious to one of ordinary skill in the art to substitute the hair growth stimulant taught by Gibson with 5-alpha reductase inhibitor at the time of the invention was made when Gibson's teaching is taken in view of Bazzano's or Schostarez's teaching. Because each patentee (Bazzano or Schostarez) teaches that 5 alpha reductase inhibitor is the effective hair stimulants can be used effectively in combination with minoxidil to improve its antialopecia effects.

As mentioned in 102 rejection (supra), Bazzano teaches that minoxidil and retinoid(a penetration enhancer) with progesterone(inherently 5-areductase inhibitor), see 102 rejection above.

Schostarez also teaches that minoxidil analog (5-fluoro minoxidil) is admixed with 5 alpha reductase inhibitor (i.e. finasteride) beneficially for treating alopecia, see column 3, lines 49-57. Schostarez also teaches that penetration enhancers (e.g. oleyl alcohol) can be effectively added to enhance its penetration so that the active ingredient can be delivered to the site of action (hair follicle) effectively, see column 4, lines 45-50 and

column 5, lines 10-15. At column 4, lines 51-56, Schostarez teaches that minoxidil can be substituted with 5-fluoro minoxidil so that conventional process of making topical composition can be incorporated and applied into the patent.

Thus, one would have been motivated to modify these teachings together to formulate the most effective topical composition wherein the enhanced therapeutic efficacy is achieved by delivering the active agents into the site of action efficiently and lowering the therapeutic dose of each component via utilizing different biological pathway and potentiating other component's activity so that one could have maximized therapeutic efficacy while reducing the unwanted side effect, which usually associated with high therapeutic dose used.

As to the claims ,7-10,16 and 18-21, the article of manufacture including the said composition and label for its intended use to promote cosmetic and pharmaceutical advantageous utilities, and the specific dosage amount and ratio required by the instant claims have been considered to be within the scope of these references because each active ingredient is well known and documented in the art. The determination of effective dosage regimens required by the instant claims are considered to be within the level of the ordinary skilled artisan, and because the minor variations including the selection of optimal dosages or variable applications in order to determine the most effective treatment is commonly practiced and obvious . Applicant's claims 8-10, 19-21 differ in that they require informational means instructing the reader in the cosmetic or pharmaceutical use of the said combination to maintain healthy hair or to induce hair growth. Judicial notice is taken that the packaging and labeling instructing use of a

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composition is old and well known, for example, see Rogain® (minoxidil 2%) and the label therein. Especially, the use of each active ingredient in separate or in combination is well known in the art as evidenced by the cited references above. The difference between the claimed and prior art articles is the printed matter on the label or other informational means indicating the intended use(already known) of the composition. However, the printed matter on the label or other informational means does not possess a "functional relationship" with the article of manufacture and is, accordingly, not granted any patentable weight. Thus, the claimed invention would have been obvious to one of ordinary skill in the art at the time of applicant's invention made. One would have been motivated to include the context specifying its advantages on the label to increase marketability and industrial value.

f. Claims 11 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bazzano (US 5183817) in view of Grollier et al(US 6,333,057).

As aforementioned immediately above, Bazzano teaches that minoxidil and retinoid with 5 alpha reductase inhibitor such as progesterone in a vehicles(e.g. propylene glycol, ethanol), see 102 rejection above.

Applicant's claims differ because they require a sunscreen.

However, it would have been obvious to one of ordinary skill in the art to add the sunscreen to the Bazzano's hair growth composition when Bazzano is taken in view of Grollier et al because Grollier et al teach the addition of sunscreen into the topical hair growth formulation; see claims and examples.

One would have been motivated to add the sunscreens into the topical hair growth composition comprising minoxidil, 5 α -reductase inhibitor and penetration enhancer, with reasonable expectation of success because the sunscreen protects the hair from damage of lackluster, discoloration or fading due to the sun, particularly U.V light. And also the sunscreen may retard and protect the scalp of alopecia subjects which is directly exposed to the possibly adverse effects of UV radiation in addition to , in the case of some of the sunscreen agents, improved solubilization of the minoxidil to be obtained as suggested in Grollier's reference, see Grollier's patent: column 2, lines 2-15.

Thus, one would have been motivated to do so because adding sunscreen into a hair growth composition improves cosmetic appeal and pharmaceutical quality as suggested in the cited reference.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same (or similar) ingredients and share common utilities, and pertinent to the problem which applicant is concerning. MPEP 2141.01(a).

(11) Response to Argument

In response to the appellant's argument, appellant is reminded that the claims are direct to a composition set forth above and it's use in the treatment of alopecia the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed

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invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In response to the appellant's argument, the use of a negative limitation excluding the characteristics of the prior art products are permitted when the product is part of the appellant's own invention. However, appellant can not exclude the product if the product is not included as the appellant's invention in the original disclosure.

MPEP(see 2173.05(i)) clearly states that any negative limitation or exclusionary proviso must have basis in the original disclosure. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 112, first paragraph as failing to comply with the written description requirement.

As mentioned by appellant , said new matter rejection was not applied in the previous office action(paper 22) right after the amendment(paper 20) was filed because of misinterpretation of patent laws and rules. However, the delayed prosecution is resulted unintentionally but purposely to fulfill the completion of accurate examination. It is still an examiner's responsibility to examine the application accurately by applying correctly interpreted patent laws and rules before issuance. Thus, it deems to be a proper practice to raise all the issues remained in the question or required to be clarified.

In response to appellant's argument that newly amended recitation(i.e. non-retinoid penetration enhancer) would have clarify that the claim term 'penetration

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enhancer" does not include BAZZANO's retinoid compounds. Appellant also allegedly states that the examiner estopped from contracting her earlier factual findings. Appellant also allegedly states that Bazzano herself calls PEG-ethanol an inert "vehicle."

Bazzano at claim 24. This statement is not correct because Bazzano calls PEG-ethanol an "vehicle" not inert vehicles(emphasis added). col. In contrast, Bazzano teaches that the conventionally known pharmacodynamic additives or carriers are used to prepare the patented composition of Bazzano's. Since PEG-ethanol are conventionally known to be vehicles(carriers) but also known to be penetration enhancers, one would have envisaged the selection of the pharmacodynamically active carriers among propylenen glycol or ethanol to improve the quality of the patented product since they are known at the time of the invention as effective penetration enhancers. The examiners provided several supporting documents to prove the examiner's allegation. For instance, Rajadhyaksha(US5482965, col. 3, lin 31) Mikulak et al(1998, abstract only), Zupan(US4440777, col.4, line 37), Gobson(US5015470, col. 14) are provided throughout the prosecution to support the examiner's allegation which informs ethanol and propylene glycol as commonly known penetration enhancers.

Therefore, latter finding of retinoid as being a penetration enhancer is better teaching in additional to the teaching of propylene glycol or ethanol as envisioned as effective pharmacodynamically active vehicles(i.e. penetration enhancing agents).

Appellant can not pick and choose propylene glycol or ethanol to be excluded from the list of possible penetration enhancers for his convenience, especially when the claims are drafted broadly as shown. Or appellant can not pick and choose retinoid to

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be included in the list of penetration enhancers so that he can later exclude retinoid enhancers from his invention to obviate the anticipatory rejection.

In response to appellant's argument that allegedly states that Gibson or Zupan fails to enable the claimed invention, Gibson or Zupan's teaching is fully enabling the claimed invention wherein the penetration enhancers suggested in the patent are well recognized by the skilled artisan and Gibson or Zupan specifically exemplifies number of compounds listed as penetration enhancers which shares common chemical structures and their functions(i.e. improving the delivery of the active drug into the target site) as the penetration enhancers. Thus, it would not difficult to measure the scope of the claimed invention. Thus, appellant's argument is not persuasive. Furthermore, appellant himself broadly claims a penetration enhancer as his invention. The argument made by appellant regarding Gibson or Zupan's teaching is contradicting to himself.

For the reasons set forth above, the claimed invention is not patentably distinct over the cited reference.

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VICKIE KIM
PRIMARY EXAMINER

Vickie Kim
Patent examiner
Art unit 1614
June 24, 2004

Respectfully submitted,

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